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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.     | CONFIRMATION NO. |
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| 10/037,110      | 10/22/2001  | Patrizia Caldirola   | 13425-052001 / 00382-US | 5944             |

7590

11/05/2002

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EXAMINER

MCKENZIE, THOMAS C

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application N .

10/037,110

Applicant(s)

CALDIROLA ET AL.

Examiner

Thomas McKenzie Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 18 23 is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-16, 22 and 24-27 is/are rejected.
- 7) ☒ Claim(s) 10 and 19-21 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. This action is in response to an application filed on 10/22/01. There are twenty-seven claims pending and twenty-seven under consideration. Claims 1-21 are compound claims. Claim 22 and 23 are a composition claim. Claims 24-27 are use claims. This is the first action on the merits. The application concerns some 1-sulfonylindole compounds, compositions, and uses thereof.

#### ***Priority***

2. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Sweden on 10/20/00. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter.

#### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a disease mediated by the serotonin-related 5-HT<sub>6</sub> receptor" is indefinite. What are these disorders? In line 27, page 1 and in lines 20-22, page 2 Applicants list some specific diseases they intend to treat. However, these passages use open language and do not specifically

identify which diseases fall into this category. The Examiner suggests listing the diseases that Applicants' intend to treat in the claims being mindful of enablement requirements for drug abuse and Parkinson's treatment.

4. Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a CNS disorder" is indefinite because all this does is provide the location of the disease. Lines 20-21, page 3 list schizophrenia, Parkinson's, and depressions as CNS disorders. Are these all? Is ADHD or drug abuse such a disorder? How about brain cancer, ALS, or bipolar disorder?

5. Claims 24-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the indole analogs such as present here. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of respiratory diseases

generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. In addition, it is presumed that prevention of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted. The Examiner suggests deletion of the word "prophylaxis".

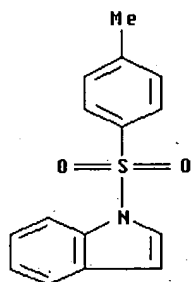
***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

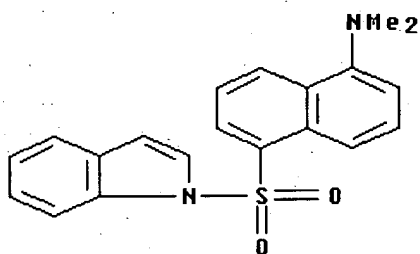
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

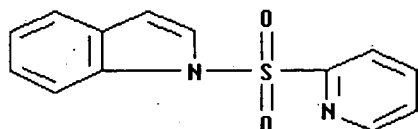
Claims 1, 2, 4, and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Illi (Synthesis). The compound shown below fits formula (I) with  $R^2 = R^3 = R^4 = R^5 = \text{hydrogen}$  and  $\text{Ar} = 4\text{-methylphenyl}$ . It has Registry number 31271-90-6 and is found in the top of the right column on page 136 of the reference. It is compound **3b**.



7. Claims 1-3, 5, 11, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Nyasse (Journal of Organic Chemistry). There are three compounds which anticipate Applicants' claims including the compound shown below fits formula (I) with  $R^2 = R^3 = R^4 = R^5 = R^7 = R^8 =$  hydrogen and Ar = 5-(dimethylamino)-1-naphthalenyl. It has Registry number 247168-06-5, is found in Table 1, page 7136, and is compound **1j**. Other anticipatory compounds are **1g** and **1h** of the reference.



8. Claims 1, 3, 6-9, 11, 12, 15, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Goulaouic-Dubois (Journal of Organic Chemistry). The compound shown below fits formula (I) with  $R^2 = R^3 = R^4 = R^5 = R^{10} =$  hydrogen and Ar = 2-pyridinyl. It has Registry number 167958-94-3 and is found in table 1, page 5969 of the reference. It is compound 7.

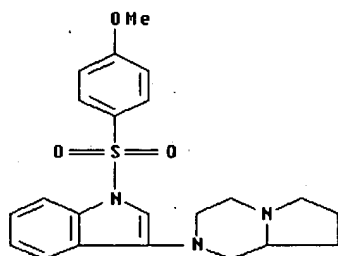


9. Claims 1, 2, 4, 11-13, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Artico (WO 96/33171 A1). The compounds **79-88** fit formula (I) with  $R^2 = R^3 = R^4 = R^5 =$  hydrogen and Ar = phenyl substituted by  $\text{NO}_2$ , Cl, and  $\text{NH}_2$ . They are found in Table 1, page 18 and pictured in Scheme 2, page 23 of the reference. Compositions of these compounds are claimed in claim 7 of the reference.

***Allowable Subject Matter***

10. Claims 18 and 23 are allowed. Claims 10, 17, and 19-21 are objected to as being dependent upon a rejected base claim. The following is a statement of reasons for the indication of allowable subject matter: The prior art does not suggest or make obvious the Ar = benzyl compounds of claims 10 and 17. Claims 1-5, 11-14, 18, and 23-25 are *per se* obvious positional isomers over Maddaford ('893). The reference teaches eleven compounds which make obvious Applicants claims including the compound with registry number 252891-64-8 shown below. The Applicant claims the compounds with a hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl radical attached to the 4 or 5 position of the indole ring. Applicants call the radical 5-aza-indolizidinyl. The reference teaches a compound with the radical attached at the 3 position. The compounds are shown in the reference in column 35, entries **6a-6k**. The difference between the claimed and taught compounds is

the position of attachment of the radical 5-aza-indolizidinyl. However, the syntheses taught in Maddaford ('893) could not be adapted to produce Applicants' isomers. Thus, the reference is not enabling for the synthesis of Applicants' compounds.



### *Conclusion*

11. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for before final amendments is (703) 872-9306. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

*Mukund J. Shah*

**Mukund Shah**  
**Supervisory Patent Examiner**  
**Art Unit 1624**

TCM  
November 1, 2002

